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Klinefelter Syndrome (KS)

KS describes a set of physical, language, and social development symptoms in males who have an extra X chromosome. Its main feature is infertility. Outward signs of KS can be subtle, so symptoms often are not recognized, and may not be treated in a timely manner. The NICHD is one of many federal agencies and NIH Institutes working to understand KS, discover why it occurs, and identify and treat its symptoms.

Common Name

- Klinefelter syndrome

Medical or Scientific Names

- Klinefelter syndrome
- 47,XXY
- XXY syndrome or condition
- XXY trisomy
- 47,XXY/46,XY or mosaic syndrome (rare variation)
- Poly-X Klinefelter syndrome, including the following rare variations:
  - 48,XXYY (or tetrasomy)
  - 48,XXXY (or tetrasomy)
  - 49,XXXXY (or pentasomy)

Klinefelter Syndrome (KS): Condition Information

What is KS?

The term "Klinefelter (pronounced *KLAHYN-fel-ter*) syndrome," or KS, describes a set of features that can occur in a male who is born with an extra X chromosome (pronounced *KROH-muh-sohm*) in his cells. It is named after Dr. Henry Klinefelter, who identified the condition in the 1940s.[1 (/health/topics/klinefelter/conditioninfo/Pages/Default.aspx#f1)]

Usually, every cell in a male's body, except sperm and red blood cells, contains 46 chromosomes. The 45th and 46th chromosomes—the X and Y chromosomes—are sometimes called "sex chromosomes" because they determine a person's sex. Normally, males have one X and one Y chromosome, making them XY. Males with KS have an extra X chromosome, making them XXY.

KS is sometimes called "47,XXY" (47 refers to total chromosomes) or the "XXY condition." Those with KS are sometimes called "XXY males."

Some males with KS may have both XY cells and XXY cells in their bodies. This is called "mosaic" (*mo-ZAY-ik*). Mosaic males may have fewer symptoms of KS depending on the number of XY cells they have in their bodies and where these cells are located. For example, males who have normal XY cells in their testes may be fertile. [2](/health/topics/klinefelter/conditioninfo/Pages/Default.aspx#f2)

In very rare cases, males might have two or more extra X chromosomes in their cells, for instance XXXY or XXXXY, or an extra Y, such as XXYY. This is called poly-X Klinefelter syndrome, and it causes more severe symptoms.[1](/health/topics/klinefelter/conditioninfo/Pages/Default.aspx#f1)

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What causes it? (/health/topics/klinefelter/conditioninfo/Pages/causes.aspx) »

What causes Klinefelter syndrome (KS)?

The extra chromosome results from a random error that occurs when a sperm or egg is formed; this error causes an extra X cell to be included each time the cell divides to form new cells. In very rare cases, more than one extra X or an extra Y is included.

« Condition Information (/health/topics/klinefelter/conditioninfo/Pages/Default.aspx)
How many people are affected/at risk?
(/health/topics/klinefelter/conditioninfo/Pages/risk.aspx) »

How many people are affected by or at risk for Klinefelter syndrome (KS)?

Researchers estimate that 1 male in about 500 newborn males has an extra X chromosome, making KS among the most common chromosomal disorders seen in all newborns.[1] (/health/topics/klinefelter/conditioninfo/Pages/risk.aspx#f1) The likelihood of a third or fourth X is much rarer: [2] (/health/topics/klinefelter/conditioninfo/Pages/risk.aspx#f2)

Prevalence of Klinefelter syndrome variants

Number of extra X chromosomes	One (XXY)	Two (XXXY)	Three (XXXXY)
Number of newborn males with the condition	1 in 500	1 in 50,000	1 in 85,000 to 100,000

Scientists are not sure what factors increase the risk of KS. The error that produces the extra chromosome occurs at random, meaning the error is not hereditary (pronounced *huh-RED-i-ter-ee*) or passed down from parent to child. Research suggests that older mothers might be slightly more likely to have a son with KS. However, the extra X chromosome in KS comes from the father about one-half of the time.[3] (/health/topics/klinefelter/conditioninfo/Pages/risk.aspx#f3)

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« What causes it? (/health/topics/klinefelter/conditioninfo/Pages/causes.aspx)
What are common symptoms? (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx) »

What are common symptoms of Klinefelter syndrome (KS)?

Because XXY males do not really appear different from other males and because they may not have any or have mild symptoms, XXY males often don't know they have KS.[1] (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f1),[2] (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f2)

In other cases, males with KS may have mild or severe symptoms. Whether or not a male with KS has visible symptoms depends on many factors, including how much testosterone his body makes, if he is mosaic (with both XY and XXY cells), and his age when the condition is diagnosed and treated.

KS symptoms fall into these main categories:

- Physical Symptoms (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#physical)
- Language and Learning Symptoms (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#language)
- Social and Behavioral Symptoms (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#social)
- Symptoms of Poly-X KS (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#polyx)

Physical Symptoms

Many physical symptoms of KS result from low testosterone levels in the body. The degree of symptoms differs based on the amount of testosterone needed for a specific age or developmental stage and the amount of testosterone the body makes or has available.

During the first few years of life, when the need for testosterone is low, most XXY males do not show any obvious differences from typical male infants and young boys. Some may have slightly weaker muscles, meaning they might sit up, crawl, and walk slightly later than average. For example, on average, baby boys with KS do not start walking until age 18 months.[3] (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f3)

After age 5 years, when compared to typically developing boys, boys with KS may be slightly:

- Taller
- Fatter around the belly
- Clumsier
- Slower in developing motor skills, coordination, speed, and muscle strength

Puberty for boys with KS usually starts normally. But because their bodies make less testosterone than non-KS boys, their pubertal development may be disrupted or slow. In addition to being tall, KS boys may have:

- Smaller testes and penis
- Breast growth (about one-third of teens with KS have breast growth)
- Less facial and body hair
- Reduced muscle tone
- Narrower shoulders and wider hips
- Weaker bones, greater risk for bone fractures
- Decreased sexual interest
- Lower energy
- Reduced sperm production

An adult male with KS may have these features:

- Infertility: Nearly all men with KS are unable to father a biologically-related child without help from a fertility specialist.[4](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f4)
- Small testes, with the possibility of testes shrinking slightly after the teen years[5](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f5)
- Lower testosterone levels, which lead to less muscle, hair, and sexual interest and function
- Breasts or breast growth (called gynecomastia, pronounced *GUY-nuh-kow-mast-ee-uh*).

In some cases, breast growth can be permanent, and about 10% of XXY males need breast-reduction surgery.[6](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f6)

Language and Learning Symptoms

Most males with KS have normal intelligence quotients (IQs)[7](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f7),[8](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f8) and successfully complete education at all levels. (IQ is a frequently used intelligence measure, but does not include emotional, creative, or other types of intelligence.) Between 25% and 85% of all males with KS have some kind of learning or language-related problem, which makes it more likely that they will need some extra help in school. Without this help or intervention, KS males might fall behind their classmates as schoolwork becomes harder.

KS males may experience some of the following learning and language-related challenges:[9](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f9)

- **A delay in learning to talk.** Infants with KS tend to make only a few different vocal sounds. As they grow older, they may have difficulty saying words clearly. It might be hard for

them to distinguish differences between similar sounds.

- **Trouble using language to express their thoughts and needs.** Boys with KS might have problems putting their thoughts, ideas, and emotions into words. Some may find it hard to learn and remember some words, such as the names of common objects.
- **Trouble processing what they hear**. Although most boys with KS can understand what is being said to them, they might take longer to process multiple or complex sentences. In some cases, they might fidget or "tune out" because they take longer to process the information. It might also be difficult for KS males to concentrate in noisy settings. They might also be less able to understand a speaker's feelings from just speech alone.
- **Reading difficulties.** Many boys with KS have difficulty understanding what they read (called poor reading comprehension). They might also read more slowly than other boys.

By adulthood, most males with KS learn to speak and converse normally, although they may have a harder time doing work that involves extensive reading and writing.

Social and Behavioral Symptoms

Many of the social and behavioral symptoms in KS may result from the language and learning difficulties. For instance, boys with KS who have language difficulties might hold back socially and could use help building social relationships.

Boys with KS, compared to typically developing boys, tend to be:

- Quieter
- Less assertive or self-confident
- More anxious or restless
- Less physically active
- More helpful and eager to please
- More obedient or more ready to follow directions

In the teenage years, boys with KS may feel their differences more strongly. As a result, these teen boys are at higher risk of depression, substance abuse, and behavioral disorders. Some teens might withdraw, feel sad, or act out their frustration and anger.

As adults, most men with KS have lives similar to those of men without KS. They successfully complete high school, college, and other levels of education. They have successful and meaningful careers and professions. They have friends and families.

Contrary to research findings published several decades ago, males with KS are no more likely to have serious psychiatric disorders or to get into trouble with the law.[10](/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f10)

Symptoms of Poly-X KS[11] (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f11)

Males with poly-X Klinefelter syndrome have more than one extra X chromosome, so their symptoms might be more pronounced than in males with KS. In childhood, they may also have seizures, crossed eyes, constipation, and recurrent ear infections. Poly-KS males might also show slight differences in other physical features.

Some common additional symptoms for several poly-X Klinefelter syndromes are listed below.

48,XXYY

- Long legs
- Little body hair
- Lower IQ, average of 60 to 80 (normal IQ is 90 to 110)
- Leg ulcers and other vascular disease symptoms
- Extreme shyness, but also sometimes aggression and impulsiveness

48,XXXY (or tetrasomy)

- Eyes set further apart
- Flat nose bridge
- Arm bones connected to each other in an unusual way
- Short
- Fifth (smallest) fingers curve inward (clinodactyly, pronounced *KLAHY-noh-dak-tl-ee*)
- Lower IQ, average 40 to 60
- Immature behavior

49,XXXXY (or pentasomy)

- Low IQ, usually between 20 and 60
- Small head
- Short
- Upward-slanted eyes
- Heart defects, such as when the chambers do not form properly[12] (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx#f12)
- High feet arches
- Shy, but friendly
- Difficulty with changing routines

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« How many people are affected/at risk? (/health/topics/klinefelter/conditioninfo/Pages/risk.aspx)
What are the treatments? (/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx) »

What are the treatments for symptoms in Klinefelter syndrome (KS)?

It's important to remember that because symptoms can be mild, many males with KS are never diagnosed ore treated.[1](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f1)

The earlier in life that KS symptoms are recognized and treated, the more likely it is that the symptoms can be reduced or eliminated.[2](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f2) It is especially helpful to begin treatment by early puberty. Puberty is a time of rapid physical and psychological change, and treatment can successfully limit symptoms. However, treatment can bring benefits at any age.

The type of treatment needed depends on the type of symptoms being treated.

Treating Physical Symptoms

Treatment for Low Testosterone[3](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f3)

About one-half of XXY males' chromosomes have low testosterone levels.[4](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f4) These levels can be raised by taking supplemental testosterone. Testosterone treatment can:

- Improve muscle mass
- Deepen the voice
- Promote growth of facial and body hair
- Help the reproductive organs to mature
- Build and maintain bone strength and help prevent osteoporosis in later years
- Produce a more masculine appearance, which can also help relieve anxiety and depression
- Increase focus and attention

There are various ways to take testosterone:

- Injections or shots, every 2 to 3 weeks

- Pills
- Through the skin, also called transdermal (pronounced *tranz-DERM-ul*); current methods include wearing a testosterone patch or rubbing testosterone gel on the skin

Males taking testosterone treatment should work closely with an endocrinologist (pronounced *en-doe-kren-AWL-oh-jist*), a doctor who specializes in hormones and their functions, to ensure the best outcome from testosterone therapy. For information on how to find an endocrinologist, see the Resources and Publications section (/health/topics/klinefelter/resources/Pages/patients.aspx).

Is testosterone therapy right for every XXY male?

Not all males with XXY condition benefit from testosterone therapy.

For males whose testosterone level is low to normal, the benefits of taking testosterone are less clear than for when testosterone is very low. Side effects, although generally mild, can include acne, skin rashes from patches or gels, breathing problems (especially during sleep), and higher risk of an enlarged prostate gland or prostate cancer in older age. In addition, testosterone supplementation will not increase testicular size, decrease breast growth, or correct infertility.

Although the majority of boys with KS grow up to live as males, some develop atypical gender identities. For these males, supplemental testosterone may not be suitable. Gender identity should be discussed with health care specialists before starting treatment.[5] (/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f5)

Treatment for Enlarged Breasts

No approved drug treatment exists for this condition of over-developed breast tissue, termed gynecomastia. Some health care providers recommend surgery—called mastectomy (pronounced *ma-STEK-tuh-mee*)—to remove or reduce the breasts of XXY males.

When adult men have breasts, they are at higher risk for breast cancer than other men and need to be checked for this condition regularly. The mastectomy lowers the risk of cancer and can reduce the social stress associated with XXY males having enlarged breasts.

Because it is a surgical procedure, mastectomy carries a variety of risks. XXY males who are thinking about mastectomy should discuss all the risks and benefits with their health care provider.

Treatment for Infertility

Between 95% and 99% of XXY men are infertile because they do not produce enough sperm to fertilize an egg naturally. But, sperm are found in more than 50% of men with KS.[6](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f6)

Advances in assistive reproductive technology (ART) have made it possible for some men with KS to conceive. One type of ART, called testicular sperm extraction with intracytoplasmic (pronounced *in-trah-sigh-toe-PLAZ-mick*) sperm injection (TESE-ICSI), has shown success for XXY males. For this procedure, a surgeon removes sperm from the testes and places one sperm into an egg.

Like all ART, TESE-ICSI carries both risks and benefits. For instance, it is possible that the resulting child might have the XXY condition. In addition, the procedure is expensive and is often is not covered by health insurance plans. Importantly, there is no guarantee the procedure will work.

Recent studies suggest that collecting sperm from adolescent XXY males and freezing the sperm until later might result in more pregnancies during subsequent fertility treatments.[7](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f7),[8](/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f8) This is because although XXY males may make some healthy sperm during puberty, this becomes more difficult as they leave adolescence and enter adulthood.

Treating Language and Learning Symptoms

Some, but not all, children with KS have language development and learning delays. They might be slow to learn to talk, read, and write, and they might have difficulty processing what they hear. But various interventions, such as speech therapy and educational assistance, can help to reduce and even eliminate these difficulties. The earlier treatment begins, the better the outcomes.

Parents might need to bring these types of problems to the teacher's attention. Because these boys can be quiet and cooperative in the classroom, teachers may not notice the need for help.

Boys and men with KS can benefit by visiting therapists who are experts in areas such as coordination, social skills, and coping. XXY males might benefit from any or all of the following:

- **Physical therapists** design activities and exercises to build motor skills and strength and to improve muscle control, posture, and balance.
- **Occupational therapists** help build skills needed for daily functioning, such as social and play skills, interaction and conversation skills, and job or career skills that match

interests and abilities.

- **Behavioral therapist**s help with specific social skills, such as asking other kids to play and starting conversations. They can also teach productive ways of handling frustration, shyness, anger, and other emotions that can arise from feeling "different."
- **Mental health therapists or counselors** help males with KS find ways to cope with feelings of sadness, depression, self-doubt, and low self-esteem. They can also help with substance abuse problems. These professionals can also help families deal with the emotions of having a son with KS.
- **Family therapists** provide counseling to a man with KS, his spouse, partner, or family. They can help identify relationship problems and help patients develop communication skills and understand other people's needs.

Parents of XXY males have also mentioned that taking part in **physical activities at low-key levels**, such as karate, swimming, tennis, and golf, were helpful in improving motor skills, coordination, and confidence.

With regard to education, some boys with KS will qualify to receive state-sponsored special needs services to address their developmental and learning symptoms. But, because these symptoms may be mild, many XXY males will not be eligible for these services. Families can contact a local school district official or special education coordinator to learn more about whether XXY males can receive the following free services:

- The Early Intervention Program for Infants and Toddlers with Disabilities (https://www2.ed.gov/programs/osepeip/legislation.html) is required by two national laws, the Individuals with Disabilities and Education Improvement Act (IDEIA) and the Individuals with Disabilities Education Act (IDEA). Every state operates special programs for children from birth to age 3, helping them develop in areas such as behavior, development, communication, and social play.
- An Individualized Education Plan (IEP (https://www2.ed.gov/parents/needs/speced/iepguide/index.html)) for school is created and administered by a team of people, starting with parents and including teachers and school psychologists. The team works together to design an IEP with specific academic, communication, motor, learning, functional, and socialization goals, based on the child's educational needs and specific symptoms.

Treating Social and Behavioral Symptoms

Many of the professionals and methods for treating learning and language symptoms of the XXY condition are similar to or the same as the ones used to address social and behavioral symptoms.

For instance, boys with KS may need help with social skills and interacting in groups. Occupational or behavioral therapists might be able to assist with these skills. Some school districts and health centers might also offer these types of skill-building programs or classes.

In adolescence, symptoms such as lack of body hair could make XXY males uncomfortable in school or other social settings, and this discomfort can lead to depression, substance abuse, and behavioral problems or "acting out." They might also have questions about their masculinity or gender identity.[9 (/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f9)] In these instances, consulting a psychologist, counselor, or psychiatrist may be helpful.

Contrary to research results released decades ago, current research shows that XXY males are no more likely than other males to have serious psychiatric disorders or to get into trouble with the law.[10 (/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx#f10)]

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« What are common symptoms? (/health/topics/klinefelter/conditioninfo/Pages/symptoms.aspx)

How is it diagnosed? (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx) »

How do health care providers diagnose Klinefelter syndrome (KS)?

The only way to confirm the presence of an extra chromosome is by a karyotype (pronounced *care-EE-oh-type*) test. A health care provider will take a small blood or skin sample and send it to a laboratory, where a technician inspects the cells under a microscope to find the extra chromosome. A karyotype test shows the same results at any time in a person's life.

Tests for chromosome disorders, including KS, may be done before birth. To obtain tissue or liquid for this test, a pregnant woman undergoes chorionic villus (pronounced *KAWR-ee-on-ik vil-uhs*) sampling or amniocentesis (*am-nee-oh-sen-TEE-sis*).[1] (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx#f1) These types of prenatal testing carry a small risk for miscarriage and are not routinely conducted unless the woman has a family history of chromosomal disorders, has other medical problems, or is above 35 years of age.

Factors that Influence when KS is Diagnosed

Because symptoms can be mild, some males with KS are never diagnosed.[2] (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx#f2)

Several factors affect whether and when a diagnosis occurs:

- Few newborns and boys are tested for or diagnosed with KS.
  - Although newborns in the United States are screened for some conditions, they are not screened for XXY or other sex-chromosome differences.
  - In childhood, symptoms can be subtle and overlooked easily. Only about 1 in 10 males with KS is diagnosed before puberty.[1] (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx#f1)
  - Sometimes, visiting a health care provider will not produce a diagnosis. Some symptoms, such as delayed early speech, might be treated successfully without further testing for KS.
- Most XXY diagnoses occur at puberty or in adulthood.
  - Puberty brings a surge in diagnoses as some males (or their parents) become concerned about slow testes growth or breast development and consult a health care provider.
  - Many men are diagnosed for the first time in fertility clinics.[3] (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx#f3) Among men seeking help for infertility, about 15% have KS;[4] (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx#f4)

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« What are the treatments? (/health/topics/klinefelter/conditioninfo/Pages/treatments.aspx)
Is there a cure? (/health/topics/klinefelter/conditioninfo/Pages/cure.aspx) »

Is there a cure for Klinefelter syndrome (KS)?

Currently, there is no way to remove chromosomes from cells to "cure" the XXY condition.

But many symptoms can be successfully treated, minimizing the impact the condition has on length and quality of life. Most adult XXY men have full independence and have friends, families, and normal social relationships.[1](/health/topics/klinefelter/conditioninfo/Pages/cure.aspx#f1) They live about as long as other men, on average.[2](/health/topics/klinefelter/conditioninfo/Pages/cure.aspx#f2)

Citations

1. Geschwind, D. H., & Dykens, E. (2004). Neurobehavioral and psychosocial issues in Klinefelter syndrome. *Learning Disabilities Research and Practice*, 19(3), 166–173.
2. Bojesen, A., Juul, S., Birkebaek, N., & Gravholt, C. H. (2004). Increased mortality in Klinefelter syndrome. *Journal of Clinical Endocrinology and Metabolism*, 89, 3830–3834.

« How is it diagnosed? (/health/topics/klinefelter/conditioninfo/Pages/diagnosed.aspx)

Other FAQs (/health/topics/klinefelter/conditioninfo/Pages/faqs.aspx) »

Klinefelter Syndrome (KS): NICHD Research Goals

The NICHD has a long history of supporting research to learn more about Klinefelter syndrome. Early research included a study that examined the cells of more than 40,000 infants for extra X chromosomes. NICHD-supported research has also explored topics including the roles of sex chromosomes in development; symptoms that arise in KS such as infertility, low testosterone, and problems with language, learning, and behavior; and how best to treat males with these symptoms. Among the areas of research that hold hope for more successful intervention and prevention in Klinefelter syndrome are studies in the following areas:

- **Genetics of Klinefelter syndrome.** The full extent of the role of the X chromosome in development is not well understood. NICHD research into disorders of the X chromosome, such as Klinefelter, Turner, and Fragile X syndromes, will reveal more about how this chromosome functions and, ultimately, how to prevent or treat symptoms in individuals with an atypical number of X chromosomes. NICHD research also aims to improve understanding of processes that can go wrong in male germ cells before fertilization or right after it, when chromosomes conjugate and divide and can leave the resulting gamete with an unusual number of sex chromosomes.
- **Pathophysiological mechanisms of KS.** KS alters hormonal balance, especially reducing testosterone levels, and exactly how this leads to infertility is unclear. Researchers are studying the mechanisms behind sperm creation and how Leydig cells function, which could identify interventions that may help preserve or restore fertility in males with KS. Investigations also include those on gonadotropin-regulated genes involved in the progression of testicular gametogenesis, Leydig cell function, and other endocrine processes.
- **Treatment strategies for KS.** Research on early interventions has successfully limited the development and severity of symptoms in KS. The NICHD is gathering evidence to identify the best interventions for learning disabilities, osteoporosis (later in life), and infertility—all symptoms of KS.

Klinefelter Syndrome (KS): Research Activities and Scientific Advances

Institute Activities and Advances

KS can influence many aspects of a person's entire life, starting very soon after conception. Therefore, many branches, sections, and laboratories at NICHD conduct research that is relevant to males with XXY or poly-KS variations.

Investigating Sex Chromosomes

KS arises from an unusual number of sex chromosomes, so research into these is important to finding ways to prevent or one day cure KS. Several components of the Division of Intramural Research (/about/org/dir/Pages/index.aspx) are studying these types of problems. The Section on Epigenetics and Development is studying how X chromosome genes influence brain, reproductive, metabolic, and immune system development. The Section on Gamete Development is studying the fruit fly for insight into early gamete cell division and how an additional X chromosome can become included. Other scientists are examining the formation of male germ cells, which are present before and after fertilization and can contain an extra X. In the Section on Clinical Genomics, scientists apply information gained from biochemical and genomic studies to clinical investigations, while also studying the biomechanical mechanisms that may contribute to genetic disorders.

Understanding KS Symptoms and Preventing or Treating Them

Infertility is a key symptom in KS and many researchers at NICHD are involved in improving understanding of how sperm production fails, starting from early in development. In the Section on Clinical Genomics, scientists developed mouse models to analyze proteins that may be key in sperm production. Other research aims to explain the network of genes involved in the renewal and differentiation of spermatogonial stem cells, meiosis, and the post-meiotic differentiation of germ cells. Researchers are also exploring mechanisms behind sperm creation and the function of Leydig cells, which produce testosterone in the presence of luteinizing hormone, and searching for new gonadotropin-regulated genes involved in testicular gametogenesis, Leydig cell function, and other endocrine processes that are disrupted in KS.

Aside from infertility, scientists are working to find ways to treat other symptoms associated with KS. The Child Development and Behavior Branch (CDBB) (/about/org/der/branches/cdbb/Pages/overview.aspx) is examining the behavioral, neurobiological, and genetic aspects of typical development and is focusing on factors that can threaten normal development. CDBB researchers are also studying prevention steps and, where intervention is needed, the most effective conditions and timing. Their findings will have implications for boys with KS, who can have some learning difficulties, such as in processing language.

Researchers in the Pediatric Growth and Nutrition Branch (/about/org/der/branches/pgnb/Pages/overview.aspx) focus on nutritional science, childhood antecedents of adult disease, developmental endocrinology, developmental neuroendocrinology, and physical growth and body composition. Topics relevant to KS males include bone weakness and gender identity issues.

Other Activities and Advances

The projects below also study aspects of health and infertility that might be related to KS.

- The Reproductive Medicine Network (RMN) (/research/supported/Pages/rmn.aspx), founded in 1990, carries out large, multicenter clinical trials of diagnostic and therapeutic interventions for male and female infertility and reproductive diseases and disorders. The network is funded through the NICHD's Fertility and Infertility (FI) Branch (/about/org/der/branches/fi/Pages/overview.aspx) and comprises seven research sites as well as a data coordinating center. The RMN currently has several ongoing clinical studies, including a clinical trial to determine a level of oxygen in culture media that improves live birth rates in couples undergoing *in vitro* fertilization.
- The National Centers for Translational Research in Reproduction and Infertility (NCTRI) (/research/supported/Pages/NCTRI.aspx) (Formerly the Specialized Cooperative Centers Program in Reproduction and Infertility Research [SCCPIR]) is a national network of research-based centers, supported by the FI Branch, that aims to promote interactions between basic and clinical scientists with the goal of improving reproductive health.
- The Learning Disabilities Research Centers Consortium (/research/supported/Pages/ldrc.aspx) includes four centers in Boulder, Houston, Tallahassee, and Seattle that conduct research on the causes and treatment of learning disabilities. Supported by the NICHD's CDBB, the centers emphasize, among other things, reading comprehension—how children understand what they read—which is difficult for some children with KS.
- The Biological Testing Facility, funded under contract with the Contraceptive Discovery and Development Branch (/about/org/der/branches/crb/Pages/overview.aspx), has developed radioimmunoassay tests to accurately measure the impact of hormone

treatment given orally, subcutaneously, or transdermally. In individuals with KS taking testosterone, accurate testing helps determine the appropriate dose.

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